SCREENING FOR COLON CANCER

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Full Disclosure

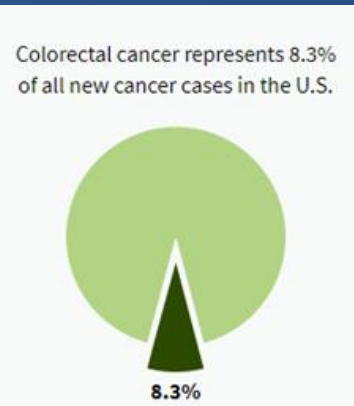
- I don't represent or receive any sort of compensation from any anyone other than my employer
- I am employed by Ivinson Memorial Hospital
  - I am paid a fixed salary
- I regularly perform colonoscopy for screening
- I am biased toward colonoscopy as the "best" form of colorectal cancer screening
- I do not get paid more/less to perform or recommend colonoscopy or any other screening method

Scope of the Problem

- 4th most commonly diagnosed cancer in US
- Over 145,000 new cases of colorectal cancer to be diagnosed in 2019
- Over 51,000 people will die from colorectal cancer in 2019
- 2nd leading cause of cancer deaths

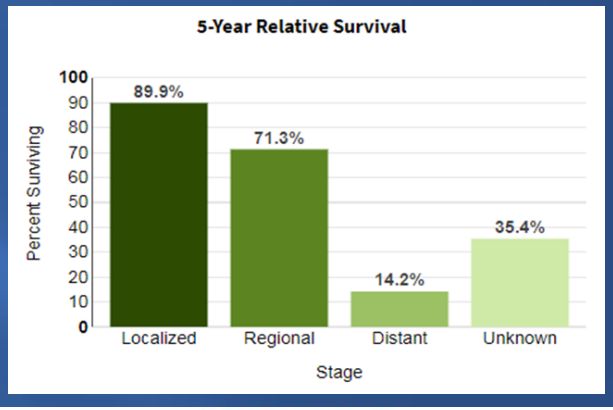
https://seer.cancer.gov/statfacts/html/colorect.html

	Common Types of Cancer	Estimated New Cases 2019	Estimated Deaths 2019
1.	Breast Cancer (Female)	268,600	41,760
2.	Lung and Bronchus Cancer	228,150	142,670
3.	Prostate Cancer	174,650	31,620
4.	**Colorectal Cancer**	**145,600**	**51,020**
5.	Melanoma of the Skin	96,480	7,230
6.	Bladder Cancer	80,470	17,670
7.	Non-Hodgkin Lymphoma	74,200	19,970
8.	Kidney and Renal Pelvis Cancer	73,820	14,770
9.	Uterine Cancer	61,880	12,160
10.	Leukemia	61,780	22,840



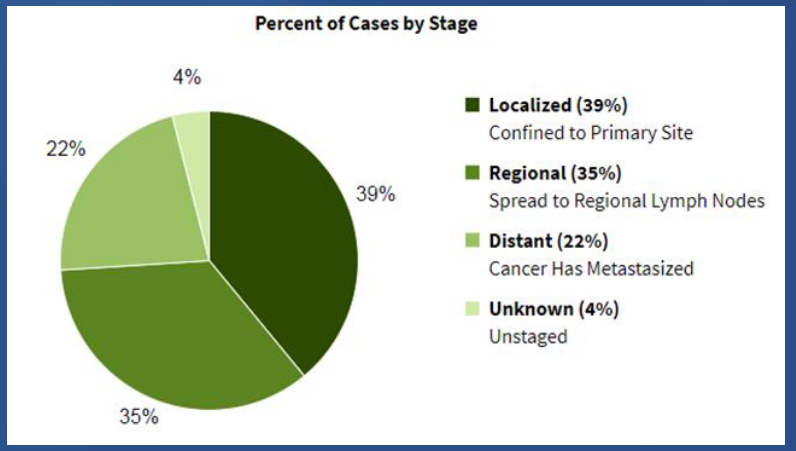
Scope of the Problem

- 1 in 20 people will get colorectal cancer (almost 5% of men and women)
- 5 year survival = 64.4% (all stages)



- Stage 1 and 2 survival is 90%
- Only 40% are diagnosed at stage1/2
- 22% diagnosed at stage 4 (14.2% survival)

https://seer.cancer.gov/statfacts/html/colorect.html



Scope of the Problem

Median Age At Diagnosis
67

- 1 in 3 people are NOT current with CRC screening
  - Over 30 million people between 50-75 years old
- 60% of deaths due to CRC could be prevented with adequate screening
- Incidence increasing in those <50yo in western countries
  - 1/10 colon cancers and almost 1/5 rectal cancers diagnosed <50yo
  - ACS now recommends starting screening at 45yo

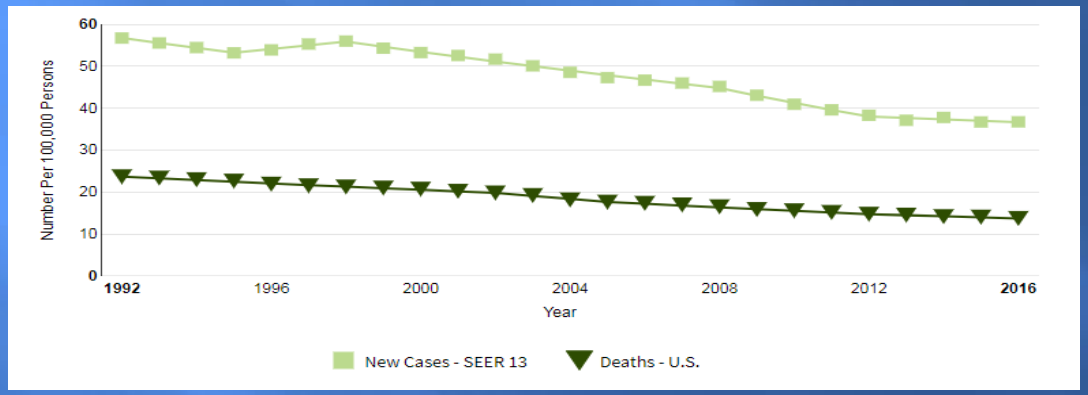
American Cancer Society:
https://cancerstatisticscenter.cancer.org/#/cancer-site/Colorectum
National Cancer Institute:
http://seer.cancer.gov/statfacts/html/colorect.html
Centers for Disease Control and Prevention
https://www.cdc.gov/cancer/colorectal/sfl/index.htm

Colon and rectal cancer and polyps

For people at average risk for colorectal cancer, the American Cancer Society recommends starting regular screening at **age 45**. This can be done either with a sensitive test that looks for signs of cancer in a person's stool (a stool-based test), or with an exam that looks at the colon and rectum (a visual exam). Talk to your health care provider about which tests might be good

The Good News

- Incidence of colorectal cancer is decreasing
- Deaths from colorectal cancer are decreasing
- 5 year survival is improving



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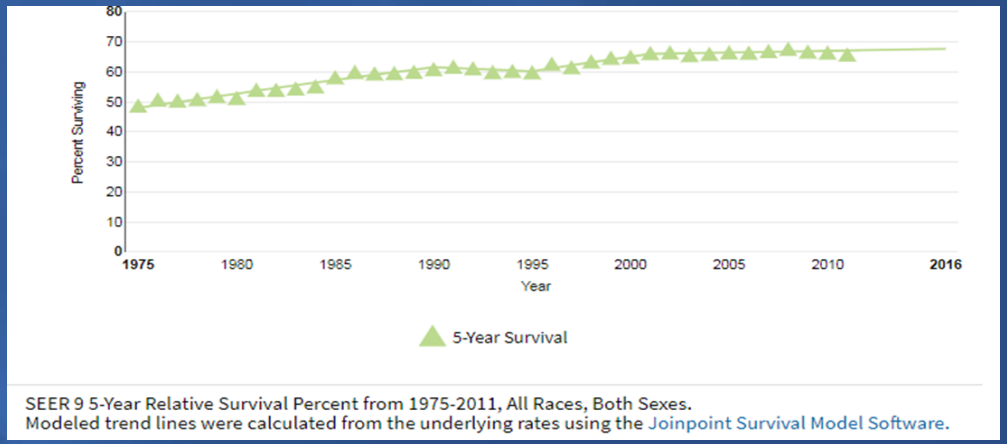
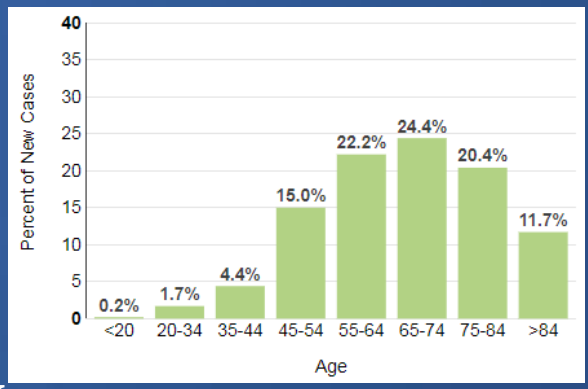
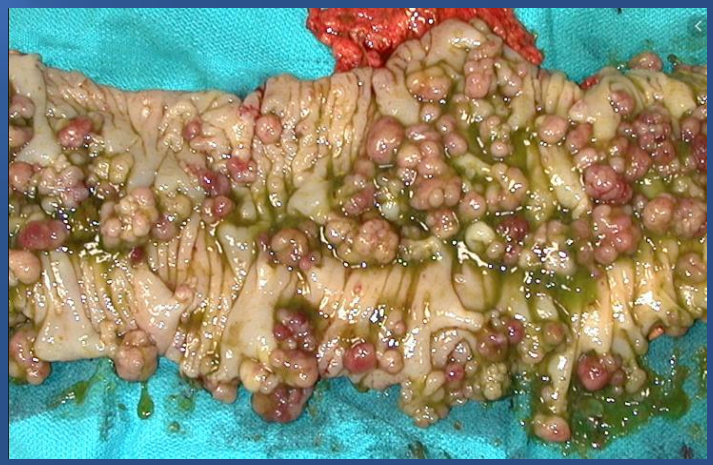


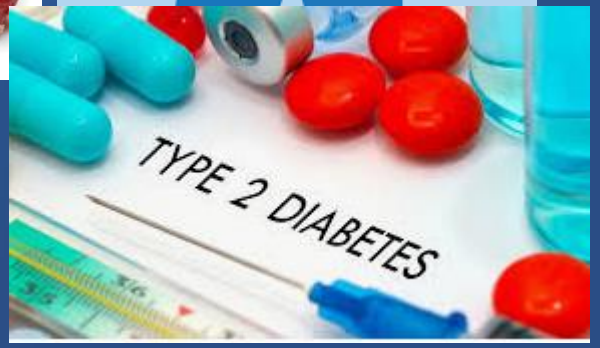
Risk Factors

- Age 50 and over
- Personal history of colorectal polyps or cancer
- Personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease)
- Family history of colorectal cancer
- Family history of inherited polyposis or Lynch syndromes
- African American ethnicity

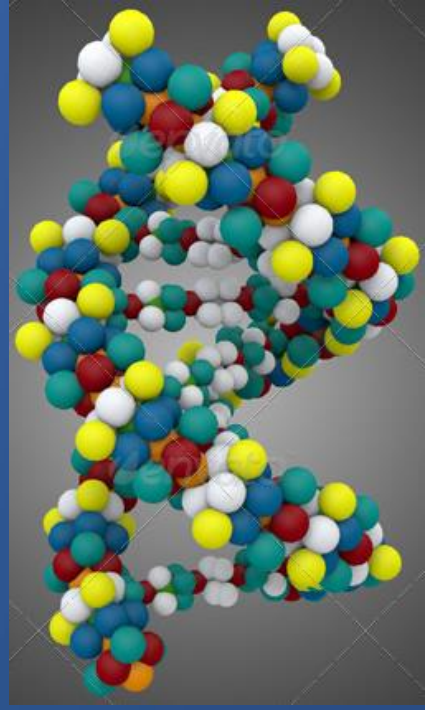




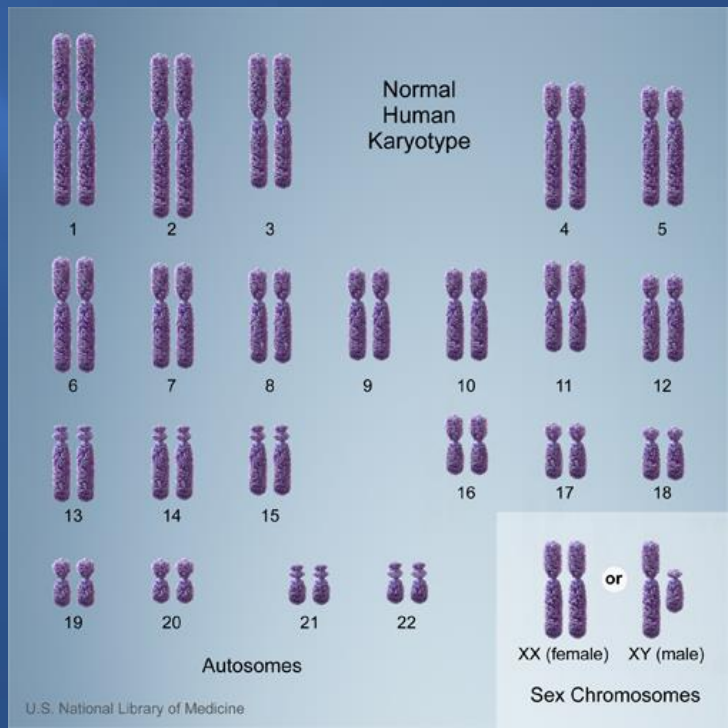
- Jews of Eastern European descent (Ashkenazi Jews)
- Type 2 Diabetes
- Diets high in red meats and low in fruits, vegetables, and whole grains
- Sedentary lifestyle
- Obesity
- Tobacco
- Heavy alcohol use



What Causes Colorectal Cancer?

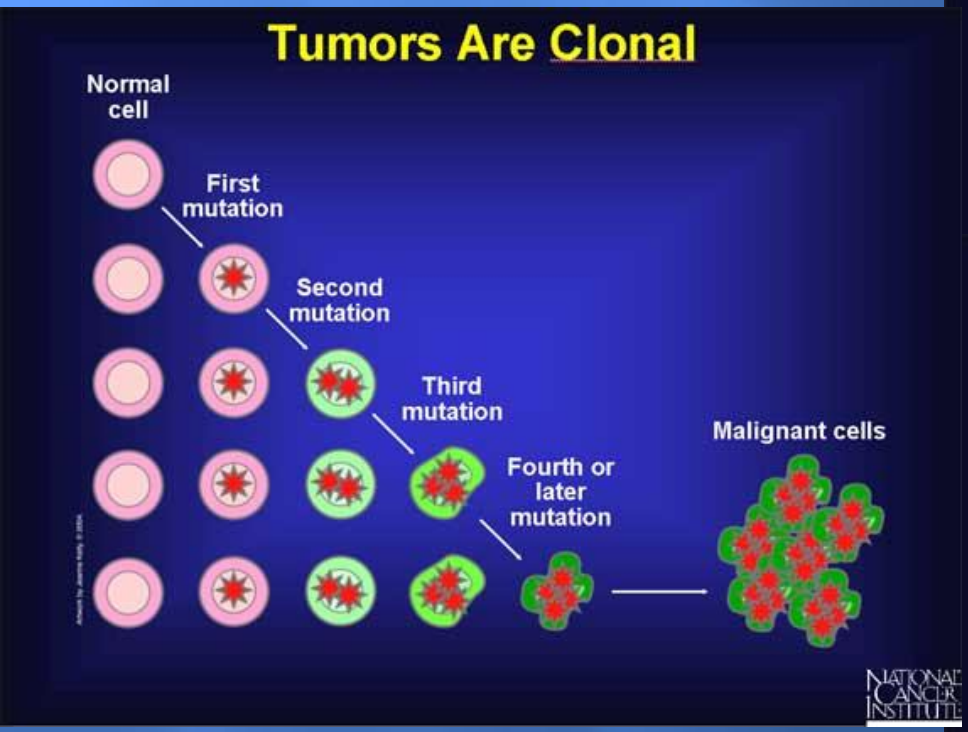


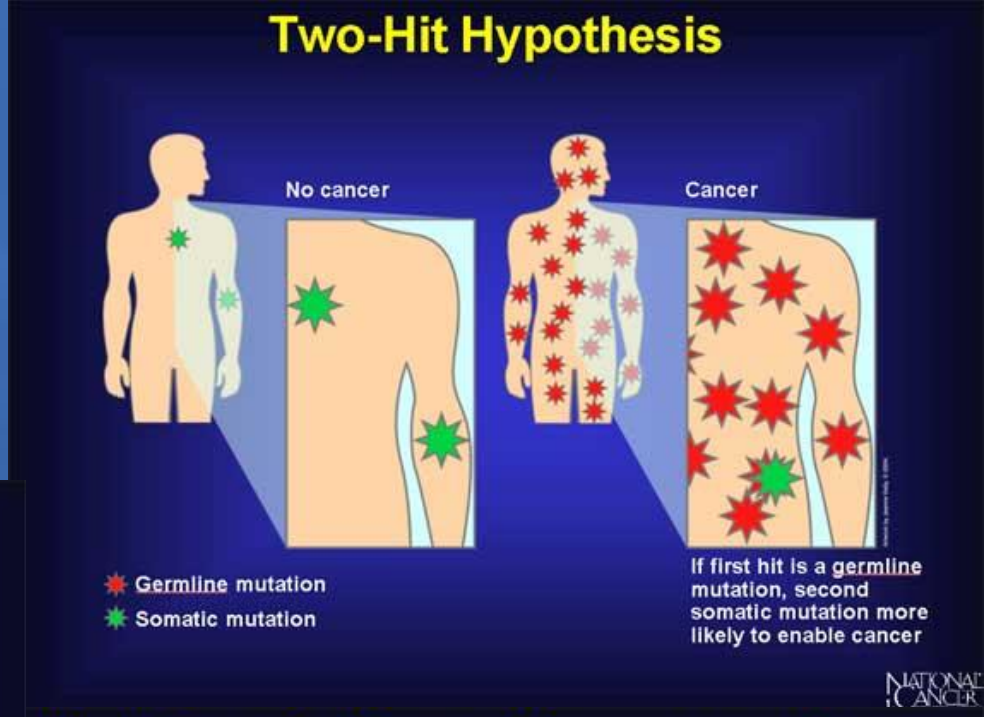
- All cancer is due to Genetic Mutations
  - Acquired
  - Inherited

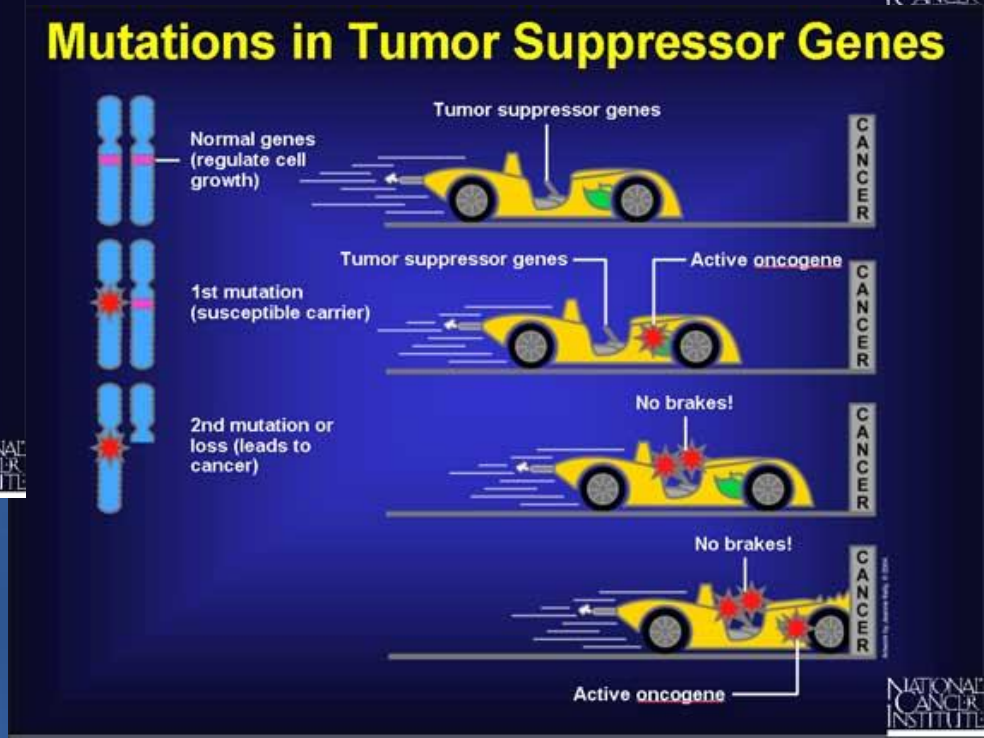


- Mutations in tumor suppressor genes lead to loss in control of cell growth and division
- Mutations in ProtoOncogenes convert the genes into Oncogenes and promote cell growth and division

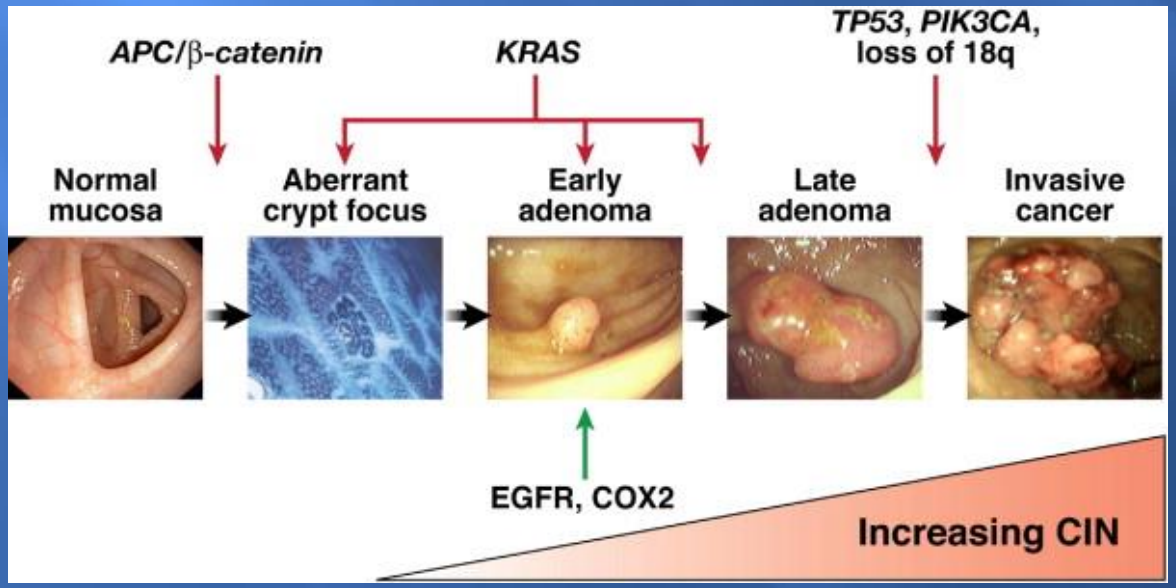
Multi-Hit Principle

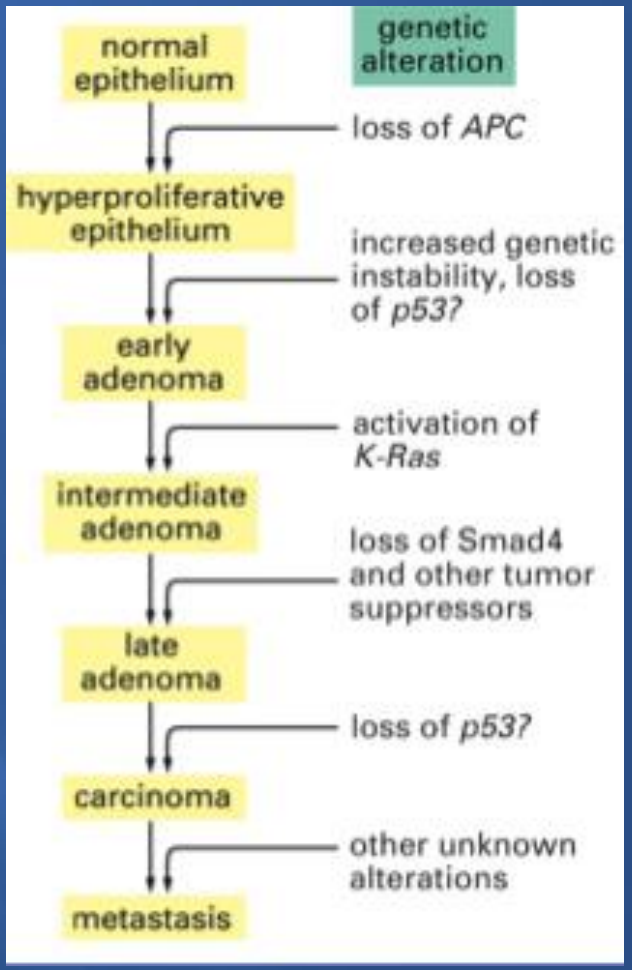


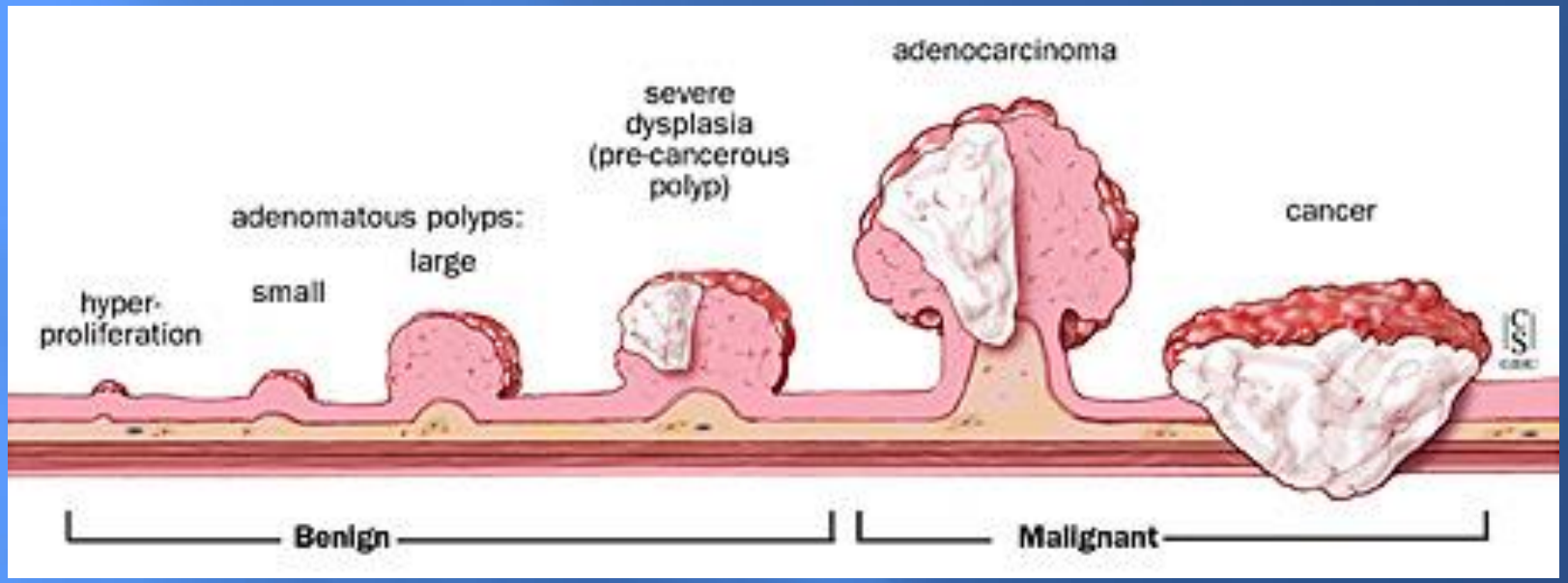




- Multiple mutations in multiple genes are required to cause colorectal cancer



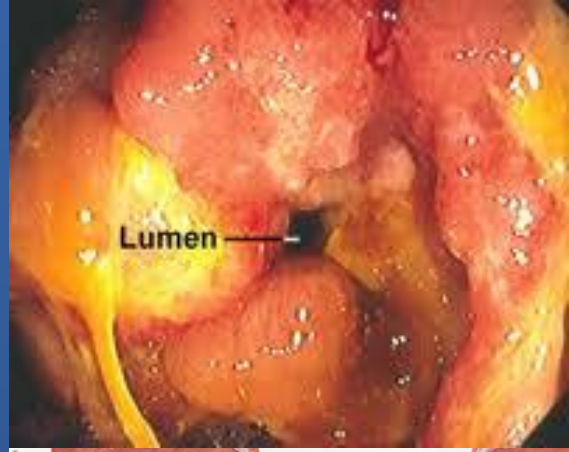


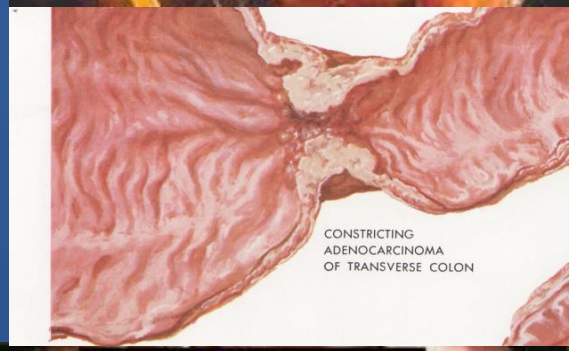


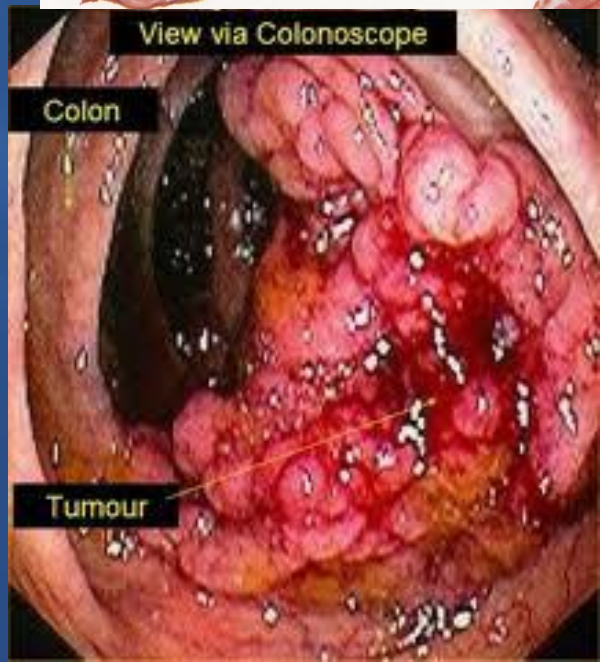
- Most mutations acquired
- Some congenital
  - Family h/o CRC
- 10 years from polyp to cancer
- Give us time to prevent CRC by removing polyps

Without Screening

- Wait for symptoms
  - Pain, rectal bleeding, obstruction, unexplained weight loss
- Cancer is advanced at time of diagnosis







Approaches to Screening

- Programmatic Screening
  - System-wide (National HealthCare Systems)
  - More organized
  - Better at tracking system-wide data
- Opportunistic Screening
  - PCP or other providers discusses screening with patient during routine visit
    - Less organized

CRC Screening in US

- Mostly opportunistic
- World's highest rates of CRC screening
  - 60% of eligible population
- Greatest reduction in CRC incidence and mortality in the world
- Due to widespread awareness and legislation (insurance coverage)
- Still, over 30% who should be getting screened are not

Principals of Widespread Screening

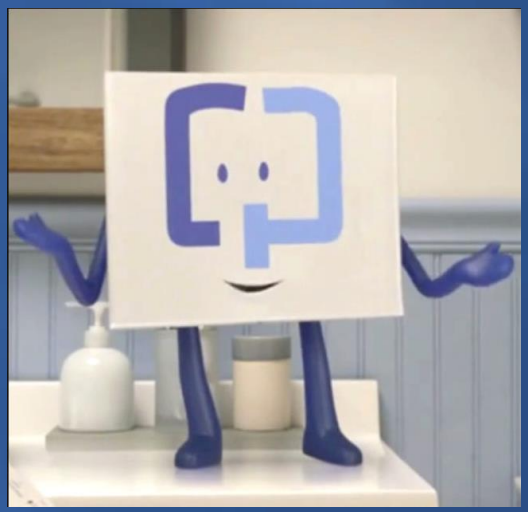
- Disease being screened for should be common in the population
- Screening test should be effective and accurate (sensitive and specific)
- Screening test should be safe
- Should be able to intervene and improve outcomes based on the screening test results
- Screening test should be "relatively inexpensive"

Screening Tests

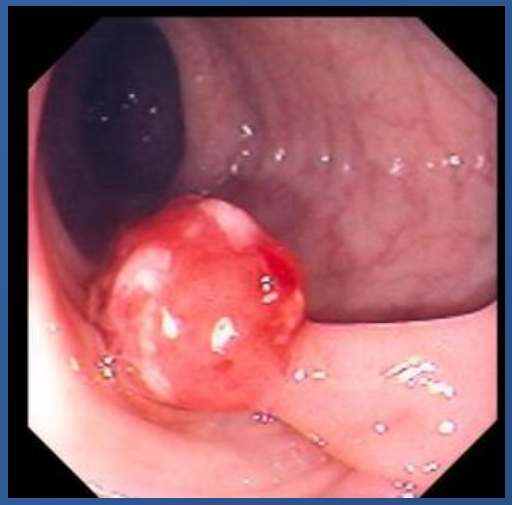
- Stool-based tests
- Imaging
- Endoscopic

Stool Based Tests

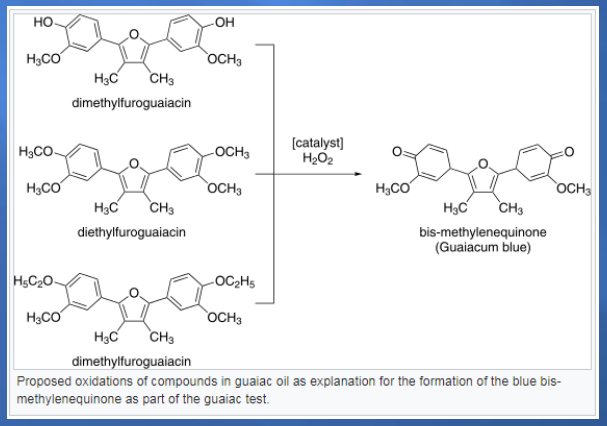
- gFOBT
- FIT-FOBT
- DNA-based testing (Cologuard)



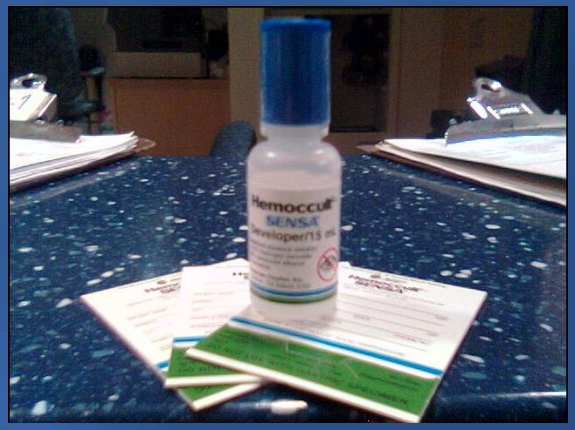
Guaiac FOBT

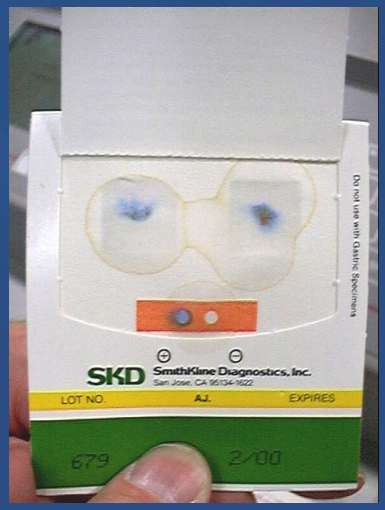


- Looks for blood (heme) in stool
- Guaiac paper
  - Plant-based phenolic compound, alpha-guaiaconic acid
    - From the wood resin of the Guaiacum tree
- Application of hydrogen peroxide to the guaiac paper creates a blue reaction product
- Heme from blood catalyzes this reaction



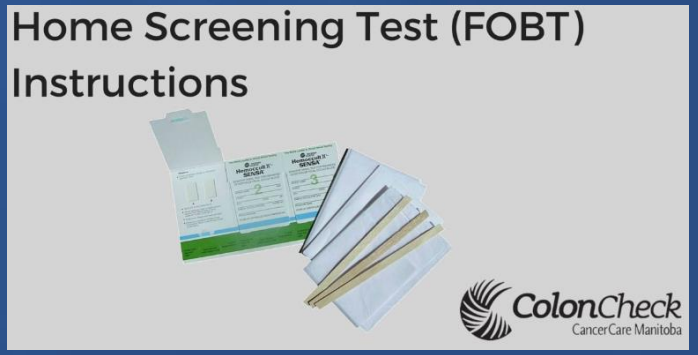
Proposed oxidations of compounds in guaiac oil as explanation for the formation of the blue bis-methylenequinone as part of the guaiac test.



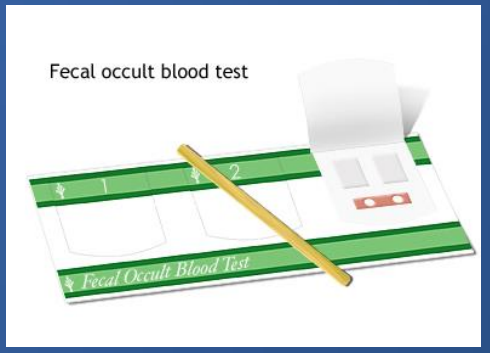


Guaiac FOBT

- Advantages
  - Cheap ($3-20)
  - Easy
  - Stool sample can be collected at home
  - Non-invasive/no sedation
  - No bowel prep
  - Widespread use can lead to improved detection of CRC



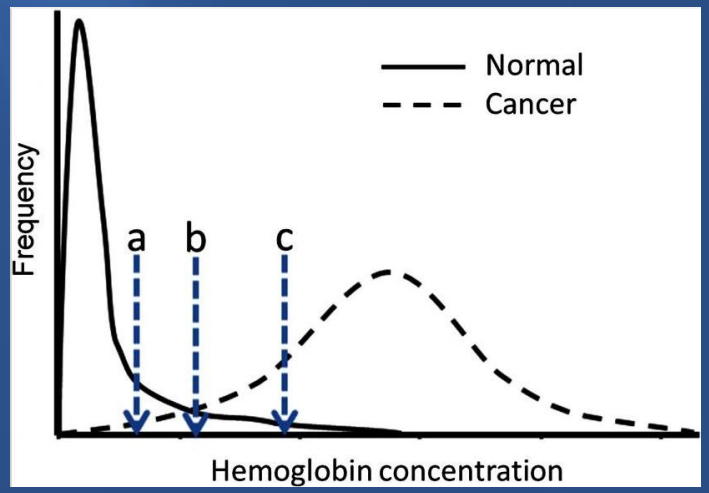
Guaiac FOBT



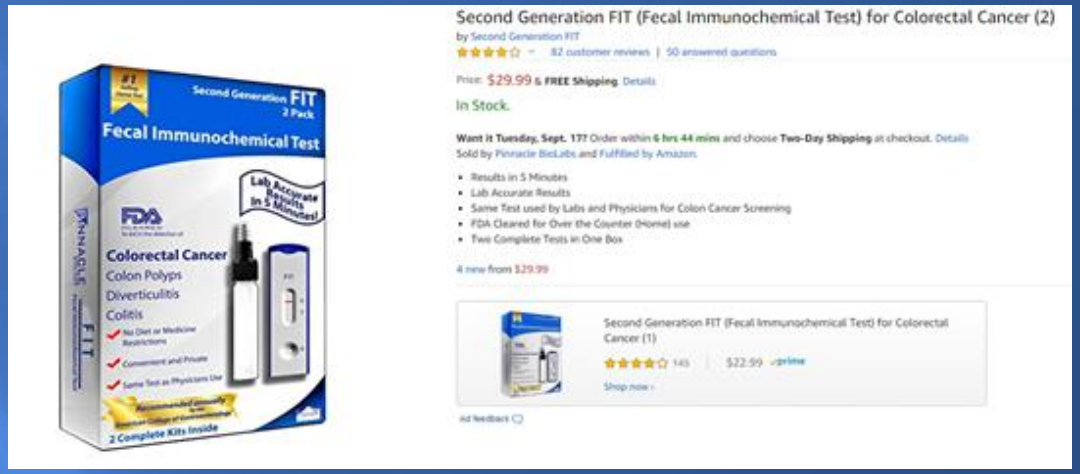
- Disadvantages
  - Poor specificity
    - Detects blood in the stool from any source in GI tract
      - Bloody noses, PUD, bleeding gums, hemorrhoids, etc
      - Detects only intact heme, not other hemoglobin breakdown products
  - False positives due to food
    - Red meat, cantaloupe, uncooked broccoli, turnips, radish, horseradish
    - NSAIDS, vitamin C can also lead to false positive results
    - These restrictions can act as a barrier to participation
  - High false negative rate (30-50% sensitivity)
  - Needs to be done annually
  - Requires 3 samples
  - Positive result = Colonoscopy
  - Patient pays more out of pocket for subsequent colonoscopy
    - Diagnostic vs screening

Immunochemical FOBT

- Fecal Immunochemical Test (FIT)
- Antibodies specific to globin moiety of human hemoglobin
- Qualitative=point of care
  - Differ in sensitivity/specificity by manufacturer
- Quantitative=laboratory based
  - Can adjust sensitivity/specificity



FIT



- Advantages
  - Cheap ($20-40)
  - Easy
  - Stool sample can be collected at home
  - Non-invasive/no sedation
  - No bowel prep
  - Widespread use can lead to improved detection of CRC
  - No pretest diet or medication changes
  - Requires only 1 stool sample
  - Better patient compliance/participation

FIT

- Disadvantages
  - Poor specificity (better than guaiac FOBT)
    - Detects blood coming from anywhere in GI tract
  - Limited sensitivity (75%)
    - Will miss polyps or early cancers if no blood is being shed in to fecal stream
  - Needs to be done annually
  - Positive result = Colonoscopy
  - Patient pays more for subsequent colonoscopy
    - Diagnostic vs screening colonoscopy

FIT-Fecal DNA

- Cologuard is the only commercially available test currently
- Detects DNA in fecal stream
  - Specifically looks for mutations in APC, K-ras, P53 genes and others

FIT-Fecal DNA

- Advantages
  - Fairly easy
  - Stool sample can be collected at home
  - Non-invasive/no sedation
  - No bowel prep
  - No dietary or medication changes
  - Complete every 3 years

FIT-Fecal DNA

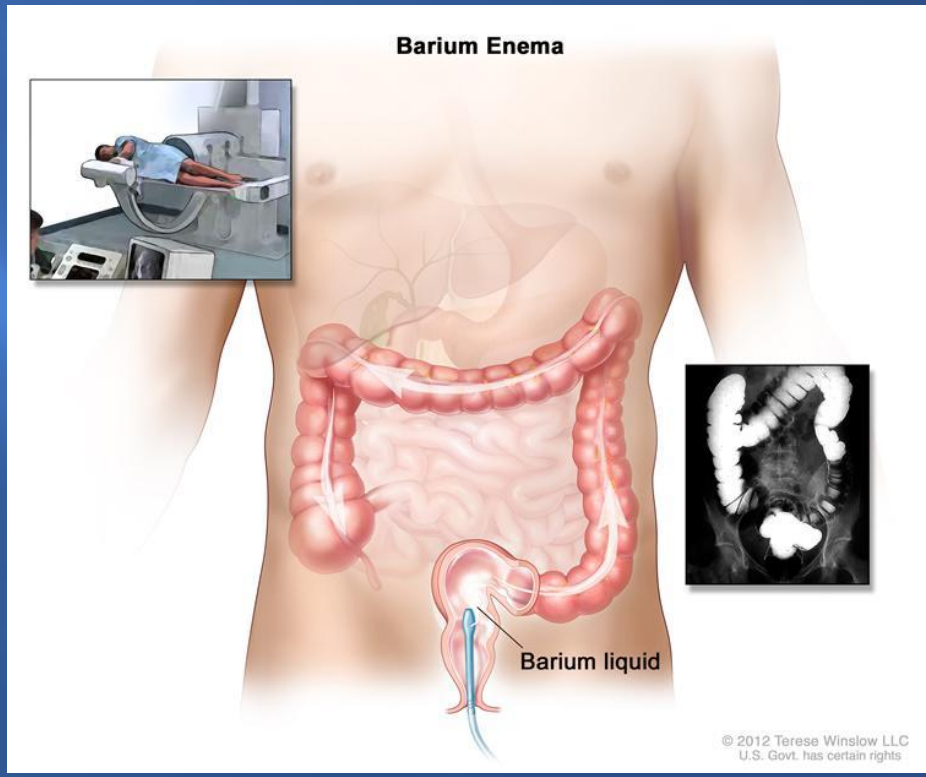
- Disadvantages
  - More expensive ($500-900)
  - Patient has to collect entire BM
  - Will miss many polyps and some cancers (false negatives)
  - High rate of false positive rates
    - More subsequent colonoscopies needed
    - Potential for higher overall costs
  - Positive result = colonoscopy
  - Patient pays more for subsequent colonoscopy
    - Diagnostic vs screening

Imaging Based Tests

- Double Contrast Barium Enema
- CT Colonography

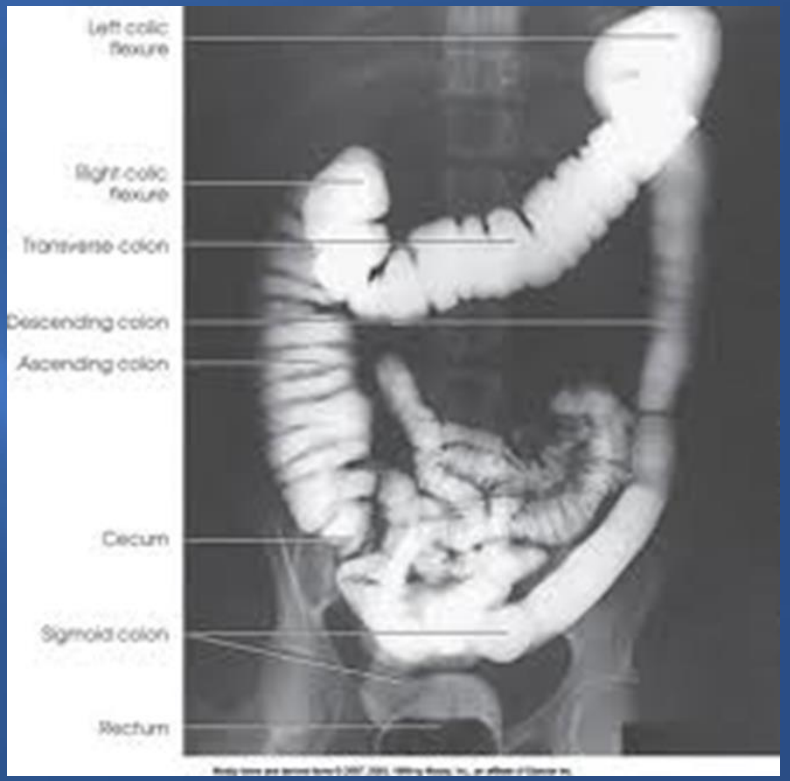
Double Contrast Barium Enema

- Contrast injected into rectum and forced into colon with hydrostatic pressure
- Requires bowel prep
- Does not require sedation
- Suitable for patients who choose not to have colonoscopy or cannot medically tolerate a colonoscopy



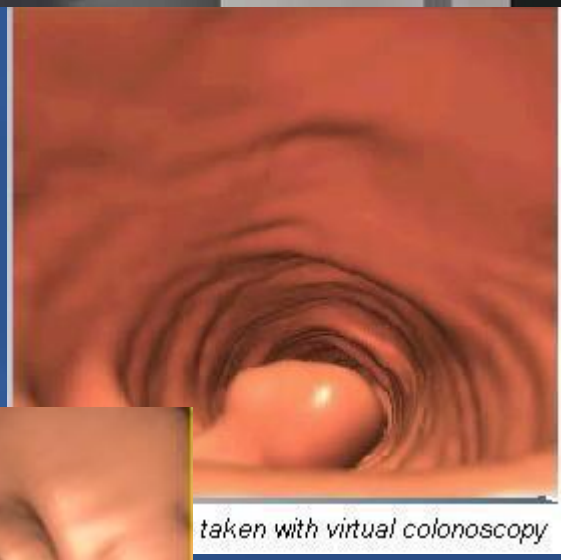
Double Contrast Barium Enema

- Will miss small (<1cm) polyps
- Will require colonoscopy if a tumor or polyp is found
- Can complete screening of right colon if colonoscopy incomplete
- Costs $250-1000
- Should be completed every 5 years

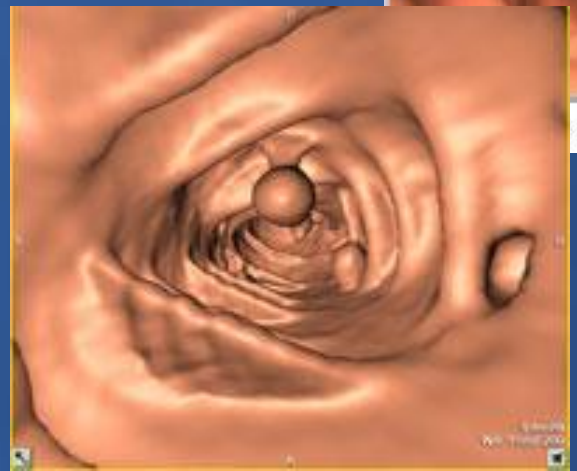


CT Colonography

- Requires bowel prep
- Does not require sedation
- Non-invasive
- Costs $500-2000
- Will require colonoscopy if any abnormalities are found
- Not available everywhere
- Should be completed every 5 years

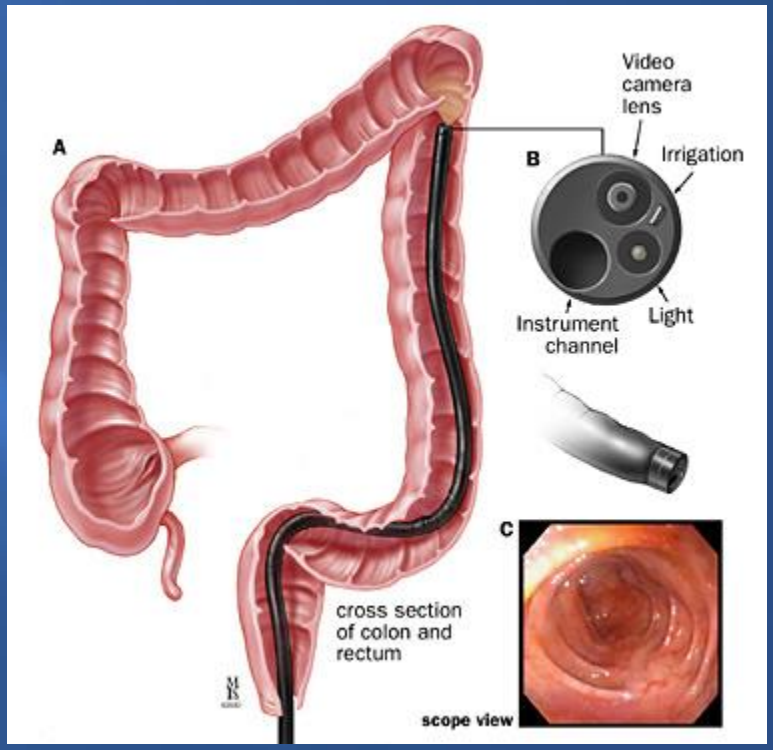


taken with virtual colonoscopy



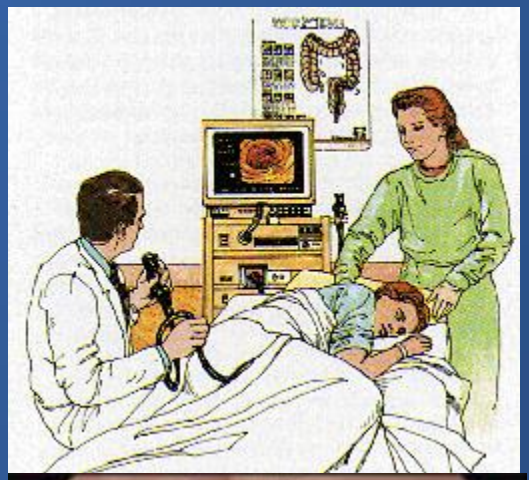
Flexible Sigmoidoscopy

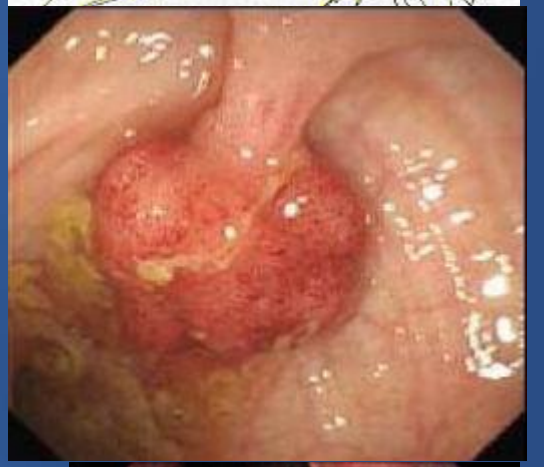
- Requires minimal bowel prep (enema)
- No sedation
- Only able to look at left colon and rectum
- Costs $800-2000
- Will need colonoscopy if polyps or tumor found
- Should be completed every 5 years

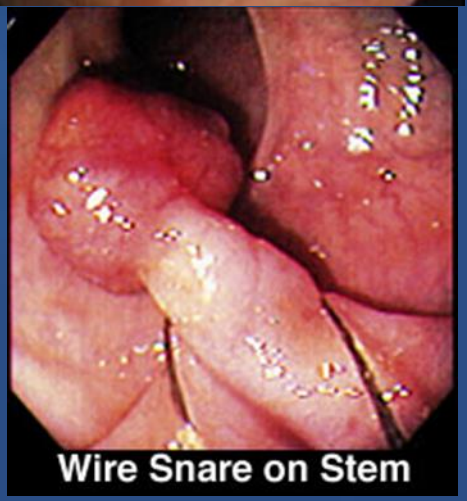


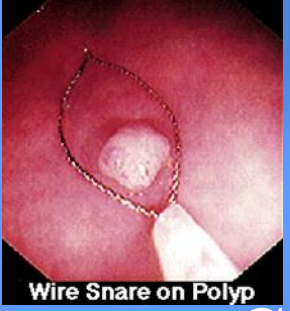
Colonoscopy

- 15,000,000/year in US
- Requires bowel prep
- Requires sedation (in most cases)
- Very small risk of colon perforation
  - 0.03-7%
- Looks at entire colon (in most cases)



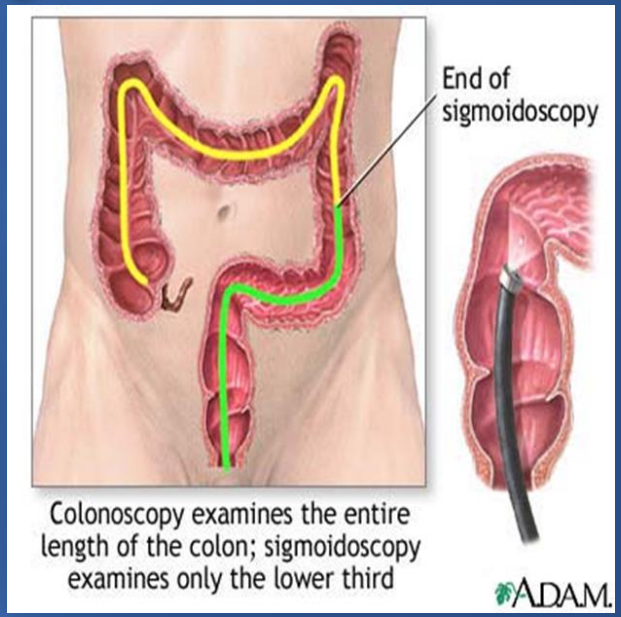


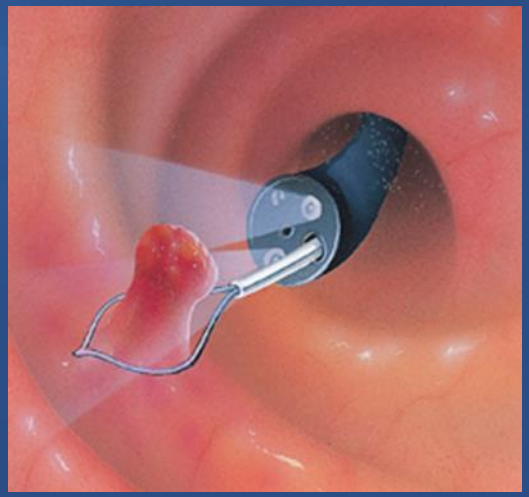




Colonoscopy

- Can perform intervention such as biopsy or polyp removal
- Highest sensitivity and specificity of all screening modalities (Gold Standard)
- Costs $1000-3000
- Should be completed every 10 years for average risk individuals
  - Every 5 years in those with FH CRC or h/o polyps





Summary of Options

Table 1. Testing Options for the Early Detection of Colorectal Cancer and Adenomatous Polyps for Asymptomatic Adults Aged 50 Years and Older

Tests that detect adenomatous polyps and cancer
FSIG every 5 years, or
CSPY every 10 years, or
DCBE every 5 years, or
CTC every 5 years
Tests that primarily detect cancer
Annual gFOBT with high test sensitivity for cancer, or
Annual FIT with high test sensitivity for cancer, or
sDNA, with high sensitivity for cancer, interval uncertain

FIT vs gFOBT

Harms, benefits and costs of fecal immunochemical testing versus guaiac fecal occult blood testing for colorectal cancer screening

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Table 1. Test characteristics of the screening tests used in the model.

Screen test	Specificity (%)	Sensitivity* (%)					
		Adenoma			CRC		
		Small (≤5mm)	Medium (6-9mm)	Large (≥10mm)	Early preclinical†	Late preclinical†	Average
gFOBT	98	2	3	8	20	52	33
FIT 50	96	4	15	37	52	83	65
FIT 75	97	3	9	31	48	81	62
FIT 100	98	2	7	28	43	77	57
FIT 150	98	2	5	25	41	76	56
FIT 200	99	1	4	21	40	76	55
Colonoscopy‡	90	75	85	95	95	95	95

CRC, colorectal cancer; gFOBT, guaiac fecal occult blood test; FIT, fecal immunochemical test.

* Sensitivity is presented per participant for fecal occult blood tests and per lesion for colonoscopy.

† It was assumed that the probability a CRC bleeds and thus the sensitivity of gFOBT and FIT for CRC depend on the time to clinical diagnosis, based on a prior calibration of the MISCAN-Colon model to three gFOBT trials.[12] This result is to be expected when cancers that bleed do so increasingly over time, starting in occult fashion and progressing to grossly visible bleeding.

‡ Colonoscopy was only used during follow-up and surveillance after a positive gFOBT or FIT. The lack of specificity of colonoscopy reflects the detection of hyperplastic polyps, which are not explicitly simulated by the MISCAN-Colon model.[28] Additional biopsy costs were assumed for procedures where biopsies were performed and in which, in retrospect, no adenomas were detected.

FIT vs gFOBT

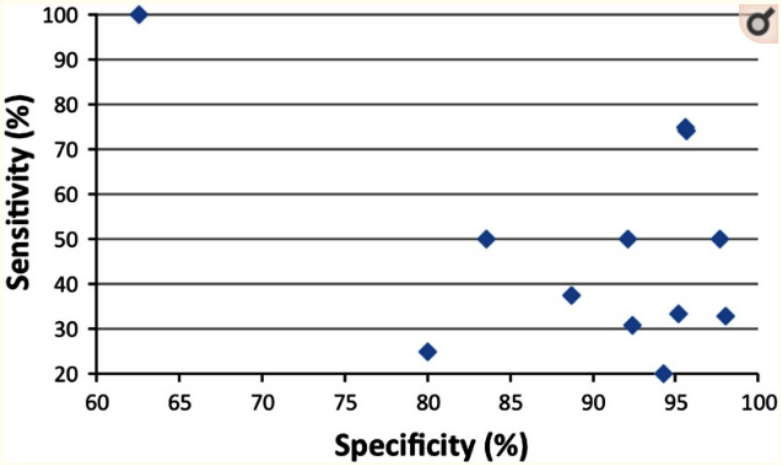


Fig. 3

Reported sensitivity and specificity for CRC of a range of gFOBT [47–58]

gFOBT

FIT

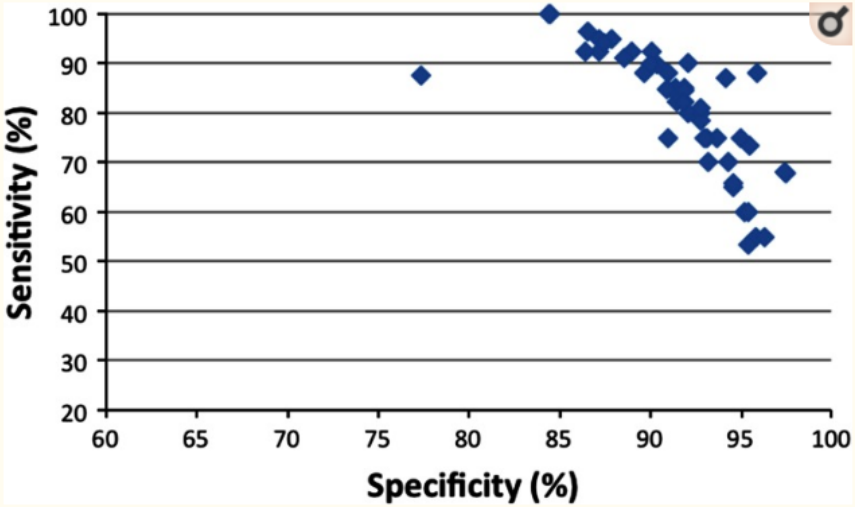


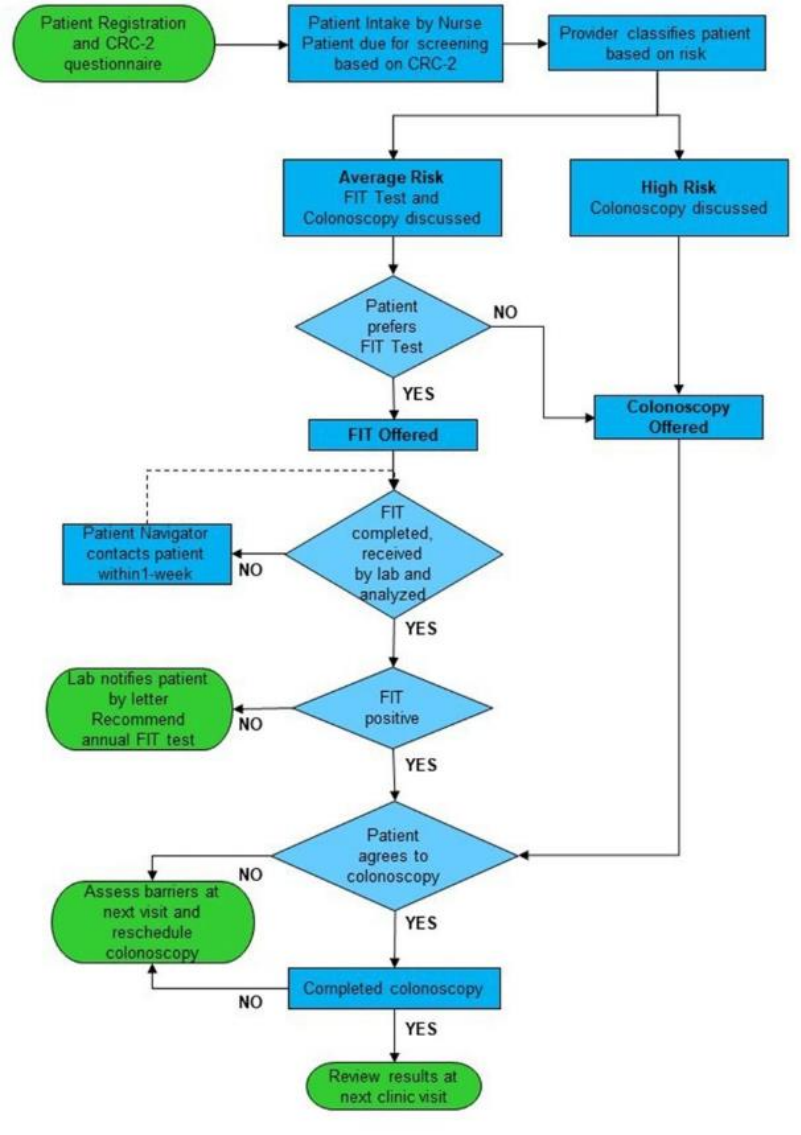
Fig. 4

Reported sensitivity and specificity for CRC of a range of FIT [38, 39, 48, 54, 55, 59–66]

Comparative Costs

- Fecal occult blood test: $3 to $40
- Fecal DNA testing: $400 to $800
- Double-contrast barium enema: $200 to $1,000
- Virtual colonoscopy: $750 to $2,000
- Sigmoidoscopy: $2,000 to $3,750
- Conventional colonoscopy: $2,000 to $3,750

CRC Screening Algorithm



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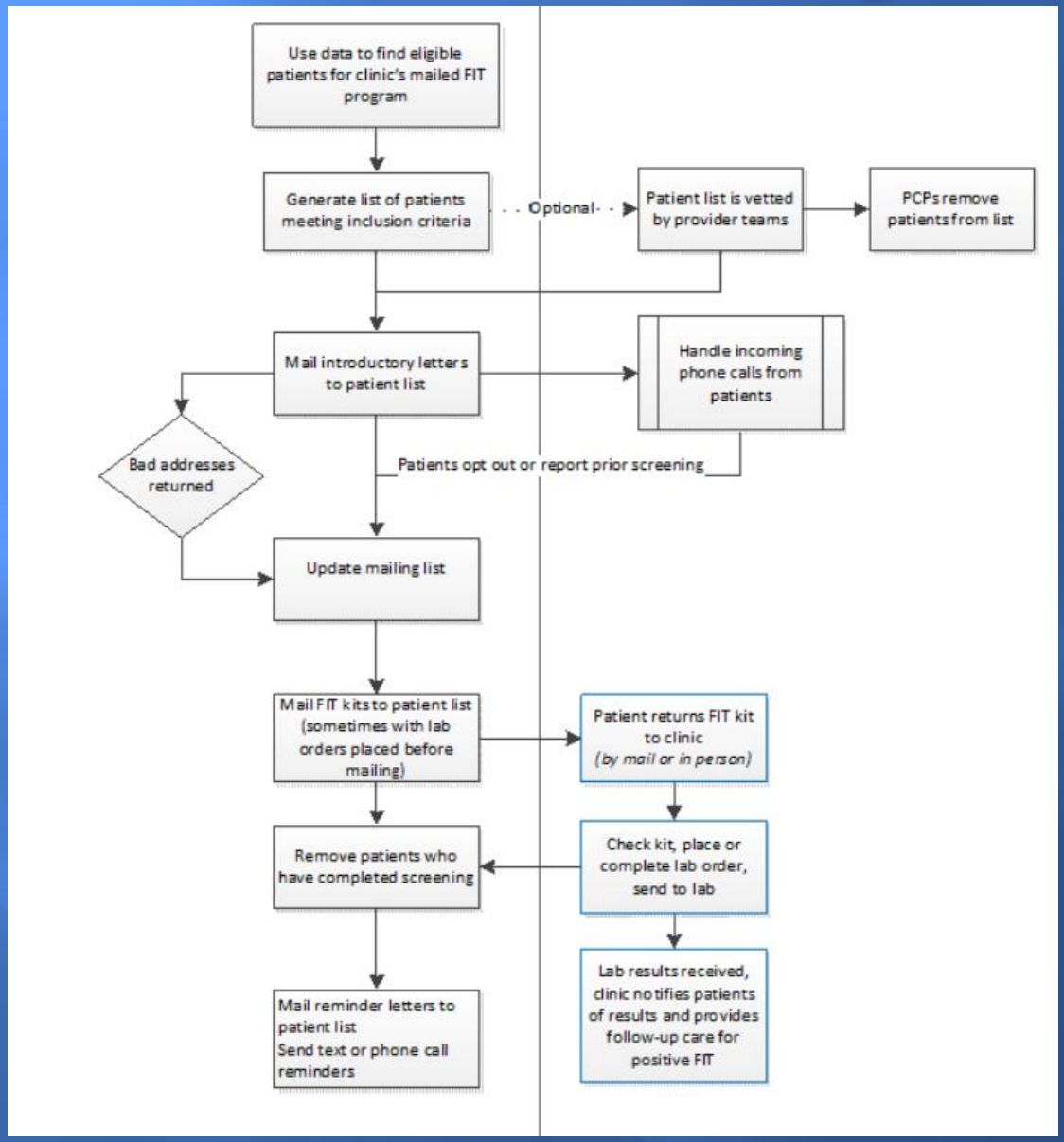
Example



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Conclusions

- Widespread colorectal cancer screening programs reduce the incidence and mortality from CRC
- CRC screening is safe and effective
- Offer CRC screening to your patients who are 50 years old or 10 years earlier than when relative was diagnosed, whichever is earlier
  - Future=45 years old?

Conclusions

- Start by recommending colonoscopy
- Recommend stool based screening (FIT or Cologuard) if patient will not get colonoscopy
  - Will need colonoscopy if positive
  - Insurance often covers less of colonoscopy as secondary test
    - Diagnostic vs screening
- The current “gold-standard” method is colonoscopy

Final Thoughts

- Have a well-developed CRC screening program in your clinic
- ANY CRC screening program is better than NO CRC screening program
  - Some are better than others
    - FIT is better than gFOBT
- Religiously screen your patients for
  - Eligibility for CRC screening
  - High risk or average risk
  - Up to date with CRC screening

Final Thoughts

CRC screening options do not apply to any patient at elevated risk of CRC due to family history, IBD, HNPCC, APC, h/o polyps, etc.

Patients at elevated risk of getting CRC REQUIRE a colonoscopy for adequate surveillance/screening

Have a CRC screening algorithm in place!!

- 3 "best" options:
  1. Recommend colonoscopy for everyone but use FIT or Cologuard testing for those that do not wish to start with colonoscopy (explain insurance implications if diagnostic colonoscopy needed)
  2. Recommend FIT or Cologuard testing but explain the weaknesses in these screening modalities and explain insurance implications if they need subsequent diagnostic colonoscopy for positive results
  3. Discuss Colonoscopy, FIT, and Cologuard on equal terms but explain the benefits and drawbacks of each as well as insurance implications of secondary diagnostic colonoscopy, if needed, and let the patient decide

Questions?